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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/758,033	11/27/1996	GARY L. CLAYMAN	INGN:022	5378

7590 06/03/2004

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/758,033	CLAYMAN, GARY L.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-20,26-32,36,37 and 146-150* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16-20,26-32,36,37 and 146-150* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed November 27, 1996, claims benefit to provisional application 60/007,810, filed November 30, 1995.

Applicant's notice of appeal and appeal brief filed March 11, 2004, has been received and entered.

A new reference previously not made of record has been identified, requiring a new rejection to be made. It is noted that the prior office action was not final, however there were more than two office actions on the merits issued by the office allowing for the request of appeal and the submission of the appeal brief. The appeal brief has been entered into the file, and the arguments presented by Applicant will be considered to the extent they apply to the new rejections set forth below.

Further, it is noted that the previous office action failed to recognize or consider newly added claims 146-150. Claims 1-14, 16-20, 26-32, 36, 37 and 146-150 are pending and currently under examination.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14, 16-20, 26-32, 36, 37 and 146-150 are provisionally rejected under the judicially created doctrine of double patenting over claims 26-88 of copending Application No. 09/968,958.

Applicant has indicated that consideration of filing a terminal disclaimer would be made once allowable subject matter was indicated. See appeal brief, page 5. Applicant's request is noted, however the rejection can not be held in abeyance. Therefore, the rejection is maintained for the reasons of record.

As noted in the previous office action, this is a provisional double patenting rejection since the conflicting claims have not yet been patented. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). In the instant case, the method set forth in claim 1 of the instant application is essentially the same as that set forth in claim 58 of '958. Further, it is noted that claim 26 of application '958 encompasses essentially the same invention as encompassed by claims 1 and 12 of '033. Dependent claims in each application set forth specific types and amounts of vectors, specific types of cancers, and specific times of administration that set forth inventions which are essentially the same in breadth between both applications.

Applicant is advised that should claim 1 be found allowable, claim146 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

In the instant case, simply indicating the mechanism on how the method works does not distinguish the claimed method from that set forth in claim 1.

Response to Amendment

Applicant notes that the declaration has been filed and the statement of Dr. Clayman supports that the invention was conceived and due diligence followed that antedates the November 1995 date of the cited references. See applicant's appeal brief, page 8. Applicant's arguments have been considered, but not found persuasive.

As indicated previously, the decision by the Board of Patent Appeals and Interferences, the declaration of Dr. Gary Clayman filed on November 18, 1999, paper number 25, under 37 CFR 1.131 has been considered to ineffective to overcome the Katayose and Srivastava references. The declaration therefore fails to satisfy the express terms of rule 131 (page 9), and does not facially inadequate to antedate the references (bridging pages 12-13). Further, the Board has indicated that upon analysis of the Katayose and Srivastava references it appears that they are "very relevant to the issue of the patentability of the instant claims under 35 U.S.C. 103 (page 13). Further, it was found by the court that the Examiner erred in withdrawing the Katayose and Srivastava references that the Board indicated to be relevant, and the references qualify as prior art under 35 U.S.C. 102(a). Applicant has not provided any new arguments or evidence that would traverse the findings of the court.

Accordingly, the rejection considering these references has been made.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-9, 13, 14, 16-20 and 36 rejected under 35 U.S.C. 102(b) as being anticipated by Liu *et al.* (IDS Reference) is withdrawn.

Applicant notes that Liu *et al.* teaches the method in an animal model, not for the treatment of humans as instantly claimed.

Examiner agrees with Applicants summary of the teaching of Liu *et al.*

Claims 1-9, 13, 14, 16-20 and 36 rejected under 35 U.S.C. 102(a) as being anticipated by Clayman *et al.* is withdrawn.

Review of the declaration provided in Exhibit J demonstrates that the Clayman *et al.* reference is not by another, therefore does not qualify as a 102(a) type reference.

Claims 1-14, 16-20, 26-32, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Roth *et al.* (5,747,469 or 6,017,524) is withdrawn.

Examiner agrees with Applicants summary of the teaching of Roth *et al.*

Claims 1-14, 16-20, 26-32, 36, 37 146, 148 and 150 are rejected under 35 U.S.C. 102(b) as being anticipated by Roth *et al.* (6,069,134).

Roth *et al.* teach a method of treating a tumor by killing the cells of the tumor through the expression of p53 (see claim 1). The vector can be deliver by a variety of vectors including adenoviral vectors, and in conjunction with known chemotherapeutic agents and protocols normally used alone in the treatment of tumors. Roth *et al.* teach to optimize deliver of specific a specific vector for different PFU and volumes and in part for the use of different types of promoters such as the CMV promoter. In the course of successfully practicing the claimed methods, Roth *et al.* teach that for effective treatment multiple times and multiple sites of delivery may be necessary to affect the entire tumor or the entire bed from which the tumor has been removed. Therefore, it would have been obvious to use the methods established in the model system for treating tumors in humans. There would have been an expectation of success

because the cells used in the model system were human, establishing that the methodology works in human tumor cells.

Claims 1-14, 16-20, 26-32, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Vogelstein *et al.* (6,677,312).

Vogelstein *et al.* teach a method wherein p53 is provided for the treatment of cancer. Vogelstein *et al.* teach that adenoviral vectors can be used, and the delivery can be tailored to the type of cancer be treated. It is noted that the allowed claims of Vogelstein *et al.* are drawn to the delivery to cells with a mutant p53, however Vogelstein *et al.* teaches that the methods can be applied to other cancers.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-14, 16-20, 26-32, 36 and 37 rejected under 35 U.S.C. 103(a) as being unpatentable over Clayman *et al.* and Liu *et al.* in view of Zhang *et al.* is withdrawn.

Since the teaching of Clayman *et al.* 1 is not by another, the combined teaching fail to teach all of the limitations set forth in the claims.

Claims 1-14, 16-20, 26-32, 36, 37 and 146-150 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava *et al.*, Cajot *et al.*, Katayose *et al.*, Will *et al.*, Liu *et al.* and Zhang *et al.*

Srivastava *et al.* teach a method of inhibiting the growth of wild-type p53 expressing LNCaP cells with adenoviral vectors encoding and expressing p53. Further Srivastava *et al.* teach that treatment with such vectors can be practiced *in vivo*. Cajot *et al.* and Katayose *et al.* provide in vitro evidence that analogous methods work in other transformed cells types reducing to practice inhibition of Hut292DM cells and MCF-1 cells. Similar to the teaching of Srivastava *et al.* Will *et al.* teach the repetitive delivery of adenoviral vectors encoding wild-type p53 for the inhibition of tumor growth in an animal. Will *et al.* demonstrate that method can be successfully applied to a variety of tumor types and that different levels of treatment could be achieved with different multiplicity of infection (figure 4). In addition, Will *et al.* teach that combination of the treatment with p53 expressing vectors with conventional cancer treatments may increase the tumor cell susceptibility to radiation or chemotherapy commonly used. Zhang *et al.* specifically teach that gene therapy can be complemented by conventional well known methods for the treatment of cancer. Therefore, given the teachings above it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine

known conventional methods for the treatment of cancer with complementing methods of gene therapy treatment. Each Srivastava *et al.*, Cajot *et al.*, Katayose *et al.*, Will *et al.*, Liu *et al.* and Zhang *et al.* represent analogous art for the treatment of cancer providing clear and specific motivation to one of ordinary skill in the art for the use of p53 expressing adenoviral vectors to inhibit tumor cell growth and the use of such gene therapy to complement conventional cancer treatment methods practiced in the art. There would have been a reasonable expectation of success to combine the method of gene therapy and conventional cancer treatment given that the methods themselves alone provide treatment by inhibiting growth or killing the cancer cells in a subject.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Claims 1-9, 13, 14, 16-20, 36 and claims 146-150 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu *et al.*

Liu *et al.* teach a method of reducing tumor burden in a mouse following the administration of an adenoviral vector encoding a wild-type p53 polypeptide. Liu *et al.* reduce to practice specifically administration to a squamous cell carcinoma in the model system used, however teach that the methods could be applied to other types of cancers. It is noted that Liu *et al.* does not reduce to practice the methods in humans, however animal models are used in the art as a means to make assessment of therapies for use in humans. The cells used in the model system are human to establish the affect in specific types of cancer and cancer cell types derived

from human subjects. The adenoviral vector used in the methods is deleted of the E1 region and has a CMV promoter for expression of the p53 inserted therein. The vector is delivered surgically to a revealed tumor in 100ul volumes in increasing log increments up to 10^{12} PFU to test efficacy. It is noted that Liu *et al.* disclose the adminstration to lines Tu 138 and Tu 177, however they teach that other cell have been used (page 3663, bottom of first column) and teach the administration to K563 cells, a lymphoblastoma cell (page 3663, second column). Therefore, it would have been obvious to use the methods established in the model system for treating tumors in humans. There would have been an expectation of success because the cells used in the model system were human, establishing that the methodology works in human tumor cells.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Claims 1-14, 16-20, 26-32, 36, 37 and 146-150 are rejected under 35 U.S.C. 103(a) as being obvious over Roth *et al.* (5,747,469 or 6,017,524).

Roth *et al.* teach a method of treating a tumor by killing the cells of the tumor through the expression of p53 (see claim 1 of '469). The vector can be deliver by a variety of vectors including adenoviral vectors (see claims 2 and 15 of '469), and in conjunction with known chemotherapeutic agents and protocols normally used alone in the treatment of tumors (see claims 3-13 of '469). Roth *et al.* teach to optimize deliver of specific a specific vector for different PFU and volumes (see claims 16-18 and 49 of '469) and in part for the use of different types of promoters such as the CMV promoter (see claims 23 and 24 of '469). Like the teaching

of Liu *et al.* Roth *et al.* does not reduce to practice the methods in humans, however animal models are used in the art as a means to make assessment of therapies for use in humans. The cells used in the model system are human to establish the affect in specific types of cancer and cancer cell types derived from human subjects. In the course of successfully practicing the claimed methods, Roth *et al.* teach that for effective treatment multiple times and multiple sites of delivery may be necessary to affect the entire tumor or the entire bed from which the tumor has been removed. Therefore, it would have been obvious to use the methods established in the model system for treating tumors in humans. There would have been an expectation of success because the cells used in the model system were human, establishing that the methodology works in human tumor cells.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

-Joe Woitach
AU1632